REMARKS

Reconsideration of the rejections set forth in the Office action mailed March 26, 2003 is respectfully requested.

I. Amendments

Claim 13 has been amended to recite a method of identifying peptoids, as recited in the final clause of the claim as filed. The claim is also amended, for clarity, to state that step (iii) involves identification of transfected cells. See e.g. page 11, lines 9-10 of the specification: "Cells that have taken up the oligonucleotide/peptoid complex can be identified".

Claim 15 has been amended to depend from claim 14, to provide proper antecedent basis for "said compartments" in claim 16.

Dependent claim 21 is amended to recite that in step (ii) of the parent claim, each said (peptoid-oligonucleotide) mixture is contacted with a plurality of distinct cell types. See e.g. page 21, lines 8-24 of the specification:

> D. Screening for Selective Transfection
>
> In one embodiment of the method, the cells or tissue used for transfection comprise (in separate compartments, or separate arrays) distinct cell types. ...
>
> One example of differential cell screening is shown in Figs. 7A-D. Four different cell lines...were transfected using a library of combinatorially synthesized peptoid delivery vehicles."

Claims 22-23 are cancelled.

In claim 29, the item "cationic sidechains found on naturally occurring amino acids" is deleted, since it is redundant to the recitation of "aminoalkyl, ammonium, guanidino, amidino, imidazole, and pyridinium" in the same claim. "Ammonium" , which is redundant to "amino" in parent claim 24, is also deleted.

No new matter is added by any of the amendments.

II. Specification

The Examiner refers to the "incorporation of essential material in the specification, e.g., page 10, lines 20-29 by reference to a foreign application or patent...or to a publicaiton, is

improper." However, the Examiner has provided no reason why the incorporated material would be considered "essential". The cited material provides background information on peptoids, but it is not critical to the enablement or written description of the claimed subject matter. Therefore, there is no reason to include the material verbatim in the specification.

The recitation in claim 23 that the "non-selected cell type is an epithelial cell" is supported in the description at, for example, page 8, line 12 and at page 21, line 15. Therefore, the objection on page 4 of the Office Action is not clear. In any event, claims 22-23 have been cancelled to expedite prosecution, rendering this objection moot.

III. Rejections under 35 U.S.C. §112, Second Paragraph

Claims 13-17 and 21-29 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

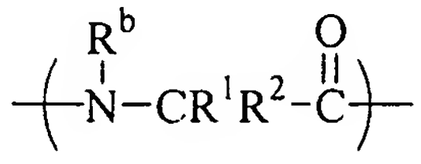
Item A. Claim 13 was objected to in that the preamble recited "screening" while the body of the claim recited "identifying". As noted above, the preamble of claim 13 has been amended to recite a method of identifying peptoids, as recited in the final clause of the original claim.

Item B. Claim 15 has been amended to depend from claim 14, to provide proper antecedent basis for the elements "compartments" (recited in claim 14) and "particles" (recited in claim 15) in claims 16 and 17 (which both depend from claim 15, and thereby from claim 14).

Item C. Dependent claim 21 is amended to remove the terms objected to; i.e. the phrase "capable of selectively delivering oligonucleotides to a selected cell type".

Item D. The Examiner objected to the term "at least one group R^b" in claim 24.

Claim 24 recites that "m is an integer selected from 2 to about 50". Therefore, the peptoid described must include at least 2 units of the structure:



Accordingly, the peptoid must include at least 2 groups R^b.

Item E. The Examiner also objected to claim 28, which recites that, in formula **I** of claim 13, "at least one R^b includes a group which is cationic at physiologically relevant pH, and at least one R^b is uncharged at physiologically relevant pH."

The reply to Item D regarding "at least one R^b" also applies to claim 28. Because "m is an integer selected from 2 to about 50" (base claim 24), the peptoid includes at least 2 groups R^b.

The Examiner also states, with respect to claim 28, that the base claim (claim 24) "does not recite a cationic or uncharged group."

The various embodiments of R^b recited in claim 24 encompass a variety of structures which "include a group which is cationic at physiologically relevant pH" or which are "uncharged at physiologically relevant pH", in accordance with claim 28. These embodiments include "alkyl, aryl, aralkyl, aralkenyl, and aralkynyl, any of which may be substituted with one or more groups X", where "X is selected from hydroxy, alkoxy, amino, guanidino, amidino, alkylamino, alkylthio, halogen, nitro, cyano, keto, aldehyde, carboxylic acid, carboxylic ester, carboxylic amide, sulfonic acid and sulfonic ester", as recited in claim 24. One skilled in the art would be able to choose among such structures those which would be "uncharged at physiologically relevant pH": for example, a structure such as "alkyl, aryl, aralkyl, aralkenyl, and aralkynyl" which is unsubstituted or which is substituted with, for example, hydroxy or alkoxy. Similarly, one skilled in the art would be able to choose among such structures those which "include a group which is cationic at physiologically relevant pH": for example, a structure such as "alkyl, aryl, aralkyl, aralkenyl, and aralkynyl" which is substituted with amino, guanidino, amidino, or alkylamino.

The Examiner made a similar objection to claim 29. Amended claim 29 recites that the cationic group of claim 28 is selected from "aminoalkyl, guanidino, amidino, imidazole, and pyridinium". Accordingly, the claim requires that at least one R^b includes a group selected from "aminoalkyl, guanidino, amidino, imidazole, and pyridinium".

Embodiments of R^b which include these groups are present in parent claim 24, as follows:

"Aminoalkyl" is encompassed by "alkyl...substituted with one or more groups X" where X is

amino. "Guanidino" and "amidino" are each embodiments of X (which may be subsitituted on any of "alkyl, aryl, aralkyl, aralkenyl, and aralkynyl"). "Imidazole" and "pyridinium" are each embodiments of "aryl", per the definition in the specification at page 13, lines 7-13, particularly lines 11-13.

In view of the foregoing, the applicants submit that amended claims 13-17, 21 and 24-29 comply with the requirements of 35 U.S.C. §112, second paragraph.

IV. Rejections under 35 U.S.C. §102(b)

Claims 13-15, 21-22, 24-25 and 27-29 were rejected under 35 U.S.C. §102(b) as being anticipated by Murphy *et al.*, *PNAS* **95**:1517, 1998. This rejection is respectfully traversed for the following reasons.

The standard for lack of novelty, that is, for anticipation, is one of strict identity. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F2d 1367, 231 USPQ 81, 90 (Fed. Cir. 1986); *In re Donohue*, 766 F2d 531, 226 USPQ 619, 621 (Fed. Cir. 1985). To anticipate a claim for a patent, a single prior source must contain all its essential elements.

A. The Invention

The applicant's invention, as embodied in independent claim 13, is directed to a method of identifying peptoids, in a library of different-sequence peptoids, which are effective in transfecting a cell with an oligonucleotide, the method comprising:

(i) contacting each peptoid in the library with an **oligonucleotide**, to form a plurality of peptoid-oligonucleotide mixtures,

(ii) contacting each said mixture with a cell;

(iii) screening each cell for transfection of the oligonucleotide, to identify transfected cells; and

(iv) identifying transfecting peptoids in mixtures contacted with transfected cells.

B. The Prior Art

Murphy *et al.* describe identification of cationic peptoids which are effective in the delivery

of plasmid DNA (pCMV-km-LUC; see "Plasmids and Cell Lines" on page 1518). The pCMV-km-LUC plasmid is described in U.S. Patent No. 6,468,986, enclosed herewith, by the same authors. According to Example 5 of the '986 patent, the plasmid has over 4,000 basepairs. (See e.g. column 43, lines 19-29: "The plasmid used in these experiments, pCMVkmLUC, was constructed by inserting the luc+gene from pSP-luc+ ...into the expression vector pCMVkm2....The sequence of pCMVkm2 is depicted in SEQ ID NO:2", which has 4328 base pairs.)

This plasmid DNA would clearly not be considered an "oligonucleotide" as that term is known to those skilled in the art. A typical definition of the term "oligonucleotide" is "a short sequence of nucleotides" (ST Nicholl, *An Introduction to Genetic Engineering*, Cambridge University Press, 1994). The more generic term "oligomer" is defined as a "general term for a short polymer most commonly consisting of amino acids (oligopeptides), nucleic acids (oligonucleotides)..." in H Lodish *et al.*, *Molecular Biology* (Scientific American Books, Inc. 1998). The present specification defines an "oligonucleotide" as "preferably between about 10 and 50, and more preferably between about 15 and 30, nucleotides in length."

There is no disclosure in Murphy of delivery of oligonucleotides. The reference does not show the step of (i) "contacting each peptoid in the library with an **oligonucleotide**".

Because the reference does not disclose all of the elements set out above in claim 13 and its dependent claims, the claims cannot be anticipated by this reference under 35 U.S.C. §102(b). In view of this, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §102(b).

V. Rejections under 35 U.S.C. §103(a)

Claims 13-17 and 21-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Murphy *et al.*, above, in view of Fasbender *et al.* (U.S. Patent No. 5,935,936). The rejections are respectfully traversed in light of the following remarks.

A. The Invention

The invention of independent claim 13, as described above, is directed to a method of

identifying peptoids, in a library of different-sequence peptoids, which are effective in transfecting a cell with an oligonucleotide. The method comprises:

(i) contacting each peptoid in the library with an oligonucleotide, to form a plurality of peptoid-oligonucleotide mixtures,

(ii) contacting each said mixture with a cell;

(iii) screening each cell for transfection of the oligonucleotide, to identify transfected cells; and

(iv) identifying transfecting peptoids in mixtures contacted with transfected cells.

B. The Cited Art

Murphy *et al.*, as noted above, describe identification of cationic peptoids which are effective in the delivery of plasmid DNA. The plasmid DNA exemplified, as noted above, has over 4,000 basepairs. There is no disclosure or suggestion of oligonucleotide delivery.

With regard to claims 23 and 26, the Examiner notes that "Murphy does not disclose the lipid steroid...attached to the peptoid". The Examiner cites Fasbender as allegedly providing the missing disclosure: "Fasbender *et al.* discloses...cationic amphiphiles containing steroid, as the commonly known DC-chol" (page 7 of Office Action).

However, the authors disclose the cationic amphiphiles, such as DC-chol, in the background discussion (see e.g. column 3, lines 6-9), and characterize these compounds as having "only modest activity" and providing uptake efficiencies which are "insufficient to support numerous therapeutic applications" (column 3, lines 27-35). Their solution to this problem is to employ a cationic amphiphile, typically a conjugate of cholesterol with an aliphatic polyamine such as spermine (column 4, lines 65-67, and following), as a mixture with a separate co-lipid, typically a phospholipid (column 4, lines 11-63).

Accordingly, the reference teaches away from the use of a steroid attached to a cationic moiety as a delivery vehicle, in the absence of a separate co-lipid as described in the reference.

In addition, the "therapeutic molecules" to be delivered, as described at column 25, lines 22-44, include (a) "polynucleotides such as genomic DNA...that encode for therapeutically useful proteins", (b) ribosomal RNA, (c) "antisense polynucleotides, whether RNA or DNA",

and (d) ribozymes. The working examples describe the delivery of protein-encoding DNA, generally in the form of plasmids having hundreds or thousands of basepairs (see e.g. column 34, line 6; column 35, line 54; column 36, line 64-65; column 39, line 18; column 41, line 55; column 42, line 35; column 44, lines 8, 28, and 46; and Example 4, "Construction of Vectors"). There is no demonstration of delivery of an oligonucleotide in the reference.

Accordingly, neither of the cited references, alone or in combination, provides any motivation to test peptoid compounds for delivery of oligonucleotides.

In view of the foregoing, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §103(a).

VI. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4403.

Respectfully submitted,

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